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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,566	06/16/2006	Francis Ignatious	PU60627	7929

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GlaxoSmithKline
GLOBAL PATENTS -US, UW2220
P. O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
05/10/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No.	Applicant(s)	
	10/596,566	IGNATIOUS ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/16/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/16/2009 has been entered. Claims 1-16 have been cancelled and new claims 17-26 have been added. Claims 17-26 are under consideration as drawn to the previously elected species: polyethylene glycol and polylactic acid.

Information Disclosure Statement

2. The Information Disclosure Statement filed o 12/16/2009 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 17-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seo et al .(WO 01/87345 A1, 2001, *of record*) in view of Cho et al .(WO 2004/022036 A1, 2004, filed on 5/30/2003), in further view of Giovanella et al. (2002/0107260, 2002, *of record*) in further view of Grochow et al .(Drug Metabolism and Disposition 1992; 20: 706-713, *of record*), and in further view of Calbiochem®(Topotecan, Hydrochloride, Cat. No. 614800 Oct. 2002).

Seo et al. teach a stable biodegradable polymer micelle-type drug composition which comprises: a modified biodegradable polymeric drug carrier micelle having a hydrophobic drug physically trapped within, wherein the drug carrier comprises an amphiphilic block copolymer having a hydrophilic poly(alkylene glycol) A block component, and a biodegradable hydrophobic polymer B block component selected from the group consisting of poly(lactic acid), poly(glycolic acid) and poly (lactic co-glycolic acid), and wherein the amphiphilic block copolymer has terminal ends modified with end groups that have an attraction or affinity for the hydrophobic drug contained in the micelle core (page 5, lines 7-17). With regards to the hydrophilic poly(alkylene glycol), the WO document teaches that hydrophilic poly(alkylene glycol) include, but are not limited to, polyethylene glycol within the range of 1,000 to 15,000

daltons (page 6, lines 17-23). With regards to the end groups, the WO document teaches that the hydrophobic polymers are capped with an end group such as a benzoyl group (page 9, lines 9-16). With regards to the hydrophobic drug, the WO document teaches that any drug having a water solubility of less than 10mg/mL can be used as a "hydrophilic drug" or poorly water soluble drug" including, but are not limited to, doxorubicin and cisplatin (page 7, line 28 to page 8, line 5).

Seo et al. do not explicitly teach that the hydrophobic polymer comprising a benzoyl end group further comprises a sulfonic acid.

Cho et al. teach amphiphilic block copolymers comprising hydrophobic blocks and hydrophilic blocks, wherein the hydrophobic block comprises a sulfonic acid which enhances the core's affinity to a hydrophobic drug (page 2, line 29 to page 3, line 8).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to modify the hydrophobic polymer taught by Seo et al .to further comprise a sulfonic acid in view of the teachings of Cho et al. One would have been motivated to do so because as taught by Cho et al .the addition of sulfonic acid to hydrophobic block polymers enhances the core's affinity to water-insoluble or poorly water soluble drugs. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by modifying the hydrophobic polymer taught by Seo et al. to further comprise a sulfonic acid in view of the teachings of Cho et al, one would further enhance the affinity to hydrophobic drugs or poorly water soluble drugs.

Seo et al. and Cho et al .do not explicitly teach that the hydrophobic drug is topotecan or a method of treating cancer comprising administering an effective amount of the complex to a patient in need thereof.

Giovanella et al. teach a method of treating a tumor in a mammal comprising administering to said mammal a water-insoluble compound, wherein the water-insoluble compound includes, but is not limited to topotecan (claim 1 of the publication). Cho et al. teach amphiphilic block copolymers comprising hydrophobic blocks and hydrophilic blocks, wherein the hydrophobic block comprises a sulfonic acid which enhances the core's affinity to a water-insoluble drug (page 2, line 29 to page 3, line 8).

Grochow et al. teach that topotecan is commercially available from the National Cancer Institute as the hydrochloride salt and has been successfully used in the treatment of tumors in animal models and clinical trials (See page 706-1st column and page 707, 1st column, Formulation and Dosage).

Calbiochem® teaches that the solubility of topotecan hydrochloride is 1 mg/ml in water.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to substitute the hydrophobic drugs as taught by Seo et al. in view of Cho et al. for topotecan hydrochloride in view of the teachings of Giovanella et al., Grochow et al. and Calbiochem®. One would have been motivated to do so because as taught by Giovanella et al. and Calbiochem®, topotecan hydrochloride is a poorly water soluble drug and falls into the class of "poorly soluble drugs" defined and used by Seo et al., i.e. any drug having a water solubility of less than 10mg/mL. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by

substituting the hydrophobic drugs as taught by Seo et al. in view of Cho et al. for topotecan hydrochloride in view of the teachings of Giovanella et al., Grochow et al. and Calbiochem® one would achieve an enhanced delivery means for poorly water soluble topotecan hydrochloride. Similarly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use topotecan hydrochloride since it has been shown to be successfully used for the treatment of various cancers.

Additionally, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer topotecan hydrochloride in the biodegradable polymer micelle-type drug composition as taught by Seo et al. in view of Cho et al. to a patient suffering from cancer in view of the teachings of Giovanella et al., Grochow et al. and Calbiochem®. One would have been motivated to do so because as taught by Seo et al., the biodegradable polymer micelle-type drug composition comprising chemotherapeutic agents has minimal side effects and shows improved bioavailability (see Abstract). Thus, one of ordinary skill in the art would have a reasonable expectation of success that by administering topotecan hydrochloride in the biodegradable polymer micelle-type drug composition as taught by Seo et al. in view of Cho et al. to a patient suffering from cancer in view of the teachings of Giovanella et al., Grochow et al. and Calbiochem®, one would achieve improved bioavailability of the drug.

Applicants argue that as noted throughout the subject specification, and as now recited in Claim 17, the present invention is directed to polymeric micelle complexes of topotecan hydrochloride, which is a water soluble bioactive agent. Accordingly, Applicants respectfully submit that Seo or Cho, whether considered alone, or in combination with any of the cited references, fail to render the present invention unpatentable.

Applicants' arguments have been considered, but have not been found persuasive because topotecan hydrochloride solubility in water as taught by Calbiochem®, is 1 mg/ml and falls into the class of "poorly soluble drugs" defined and used by Seo et al., i.e. any drug having a water solubility of less than 10mg/mL. See p. 7, lines 28-30 of Seo et al. Thus, given that Seo et al. uses drugs with topotecan hydrochloride's water solubility, the invention is obvious for the reasons set forth above and Applicants' arguments are not found persuasive.

4. No claims allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571)272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Helms Larry can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Peter J Reddig/
Primary Examiner, Art Unit 1642